

WHAT IS CLAIMED IS:

1 1. A method of treating pain comprising intravenously administering to
2 an individual in need of said treatment (a) 0.1 mg to 0.8 mg of naloxone hydrochloride salt or
3 an equivalent amount of naloxone free base, prodrug, non-hydrochloride salt, or mixture
4 thereof and (b) an amount of nalbuphine free base, hydrochloride salt, prodrug, non-
5 hydrochloride salt or mixture thereof that results in greater analgesia than administration of
6 either said naloxone hydrochloride salt or said nalbuphine alone, provided that 5 mg
7 nalbuphine free base or an equivalent amount of nalbuphine hydrochloride salt, non-
8 hydrochloride salt, prodrug, or mixture thereof, is not intravenously administered with 0.4 mg
9 naloxone free base or equivalent amount of naloxone hydrochloride salt, non-hydrochloride
10 salt, prodrug, or mixture thereof.

1 2. The method of claim 1 wherein the amount of nalbuphine
2 hydrochloride salt administered is 6.25 to 49 times greater, by weight, than the amount of
3 naloxone hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug, non-
4 chloride salt, or mixture thereof is administered.

1 3. The method of claim 1 wherein the amount of nalbuphine
2 hydrochloride salt administered is 10 to 30 times greater, by weight, than the amount of
3 naloxone hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug, non-
4 chloride salt, or mixture thereof is administered.

1 4. The method of claim 1 wherein the amount of nalbuphine
2 hydrochloride salt administered is 9 to 15 times greater, by weight, than the amount of
3 naloxone hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug, non-
4 chloride salt, or mixture thereof is administered.

1 5. The method of claim 1 wherein 1 mg to 10 mg of nalbuphine
2 hydrochloride salt is administered, or an equivalent amount of nalbuphine free base, prodrug,
3 non-chloride salt, or mixture thereof is administered, provided that 5 mg nalbuphine free base
4 is not administered with 0.4 mg naloxone free base.

1 6. The method of claim 1 wherein 1 mg to 6 mg of nalbuphine
2 hydrochloride salt is administered, or an equivalent amount of nalbuphine free base, prodrug,

3 non-chloride salt, or mixture thereof is administered, provided that 5 mg nalbuphine free base
4 is not administered with 0.4 mg naloxone free base.

1 7. The method of any of the claims 1 to 6 wherein 0.1 mg to 0.4 mg
2 naloxone hydrochloride salt or an equivalent amount of naloxone free base, prodrug, non-
3 chloride salt, or mixture thereof is administered.

1 8. The method of any of the claims 1 to 6 wherein 0.4 mg to 0.8 mg
2 naloxone hydrochloride salt or an equivalent amount of naloxone free base, prodrug, non-
3 chloride salt, or mixture thereof is administered.

1 9. A method of treating pain comprising administering intravenously to
2 an individual in need of said treatment (a) 0.1 mg to 0.8 mg of naloxone hydrochloride salt or
3 an equivalent amount of naloxone free base, prodrug, non-hydrochloride salt, or mixture
4 thereof and (b) an amount of pentazocine free base, hydrochloride salt, prodrug, non-
5 hydrochloride salt or mixture thereof that results in greater analgesia than administration of
6 either said naloxone hydrochloride salt or said pentazocine hydrochloride salt alone, provided
7 that 60 mg of pentazocine free base or an equivalent amount of pentazocine hydrochloride
8 salt, non-hydrochloride salt, prodrug, or mixture thereof, is not administered with 0.4 mg
9 naloxone free base or equivalent amount of naloxone hydrochloride salt, non-hydrochloride
10 salt, prodrug, or mixture thereof.

1 10. The method of claim 9 wherein pentazocine hydrochloride salt is
2 administered in an amount 18 to 120 times greater, by weight, than the amount of naloxone
3 hydrochloride salt, or an equivalent amount of pentazocine free base, prodrug, non-
4 hydrochloride salt, or mixture thereof is administered.

1 11. The method of claim 9 wherein pentazocine hydrochloride salt is
2 administered in an amount 18 to 50 times greater, by weight, than the amount of naloxone
3 hydrochloride salt, or an equivalent amount of pentazocine free base, prodrug, non-
4 hydrochloride salt, or mixture thereof is administered.

1 12. The method of claim 9 wherein 3 mg to 50 mg pentazocine
2 hydrochloride salt or an equivalent amount of pentazocine free base, prodrug, hydrochloride
3 salt, or mixture thereof is administered.

1 13. The method of claim 9 wherein 3 mg to 30 mg pentazocine
2 hydrochloride salt or an equivalent amount of pentazocine free base, prodrug, hydrochloride
3 salt, or mixture thereof is administered.

1 14. A method of treating pain comprising administering intravenously to
2 an individual in need of said treatment (a) 0.1 mg to 0.8 mg of naloxone hydrochloride salt or
3 an equivalent amount of naloxone free base, prodrug, non-hydrochloride salt, or mixture
4 thereof and (b) an amount of butorphanol free base, prodrug, pharmaceutically acceptable salt
5 or mixture thereof that results in greater analgesia than administration of either said
6 nalbuphine hydrochloride salt or said butorphanol alone.

1 15. The method of claim 14 wherein 0.3 to 10 times greater, by weight,
2 butorphanol tartrate salt than naloxone hydrochloride salt is administered, or equivalent
3 amount of butorphanol free base, non-tartrate salt, prodrug, or mixture thereof and/or
4 naloxone free base, non-hydrochloride salt, prodrug, or mixture thereof is administered.

1 16. The method of claim 14 wherein 0.5 to 4 times greater, by weight,
2 butorphanol tartrate salt than naloxone hydrochloride salt is administered, or equivalent
3 amount of butorphanol free base, non-tartrate salt, prodrug, or mixture thereof and/or
4 naloxone free base, non-hydrochloride salt, prodrug, or mixture thereof is administered.

1 17. The method of claim 14 wherein 0.2 mg to 2 mg butorphanol tartrate
2 salt or an equivalent amount of butorphanol free base, non-tartrate salt, prodrug, or mixture
3 thereof is administered.

1 18. The method of claim 14 wherein 0.2 mg to 1 mg butorphanol tartrate
2 salt or an equivalent amount of butorphanol free base, non-tartrate salt, prodrug, or mixture
3 thereof is administered.

1 19. A method of treating pain comprising administering, by a method other
2 than intravenous administration, to an individual in need of said treatment (a) 0.1 mg to 0.8
3 mg of naloxone hydrochloride salt or an equivalent amount of naloxone free base, prodrug,
4 non-hydrochloride salt, or mixture thereof and (b) an amount of nalbuphine free base,
5 prodrug, pharmaceutically acceptable salt or mixture thereof that results in greater analgesia
6 than administration of either said naloxone hydrochloride salt or said nalbuphine alone.

1 20. The method of claim 19 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, and naloxone are administered in amounts equivalent to
3 intravenous administration of 6.25 to 30 times greater in weight of nalbuphine hydrochloride
4 salt than naloxone hydrochloride salt.

1 21. The method of claim 19 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, and naloxone are administered in amounts equivalent to
3 intravenous administration of 10 to 20 times greater in weight of nalbuphine hydrochloride
4 salt than naloxone hydrochloride salt.

1 22. The method of claim 19 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 1 mg to 10 mg of nalbuphine hydrochloride salt.

1 23. The method of claim 19 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 2 mg to 8 mg of nalbuphine hydrochloride salt.

1 24. The method of claim 19 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 1 mg to 4 mg of nalbuphine hydrochloride salt.

1 25. The method of claim 19 wherein the method of administration is
2 mucosal.

1 26. The method of claim 25 wherein administration is nasal.

1 27. The method of claim 26 wherein the nasal administration is in the form
2 of a nasal spray or nose drops.

1 28. The method of claim 19 wherein administration is sublingual.

1 29. The method of claim 28 wherein 1 to 60 times greater, by weight,
2 nalbuphine hydrochloride salt is administered than naloxone hydrochloride salt, or equivalent
3 amounts thereof, respectively, of nalbuphine free base, non-hydrochloride salt, prodrug, or
4 mixture thereof and naloxone free base, non-hydrochloride salt, prodrug, and mixture thereof.

1 30. The method of claim 28 wherein 1 to 30 times greater, by weight,
2 nalbuphine hydrochloride salt is administered than naloxone hydrochloride salt, or equivalent
3 amounts thereof, respectively, of nalbuphine free base, non-hydrochloride salt, prodrug, or
4 mixture thereof and naloxone free base, non-hydrochloride salt, prodrug, and mixture thereof.

1 31. The method of claim 28 wherein 5 mg to 65 mg nalbuphine
2 hydrochloride salt or an equivalent amount of nalbuphine free base, non-hydrochloride salt,
3 prodrug, or mixture thereof is administered.

1 32. The method of claim 28 wherein 7.5 mg to 30 mg nalbuphine
2 hydrochloride salt or an equivalent amount of nalbuphine free base, non-hydrochloride salt,
3 prodrug, or mixture thereof is administered.

1 33. The method of claim 28 wherein 0.4 mg to 4 mg naloxone
2 hydrochloride salt or an equivalent amount of naloxone free base, non-hydrochloride salt,
3 prodrug, or mixture thereof is administered.

1 34. The method of claim 28 wherein 0.4 mg to 2 mg naloxone
2 hydrochloride salt or an equivalent amount of naloxone free base, non-hydrochloride salt,
3 prodrug, or mixture thereof is administered.

1 35. A method of treating pain comprising administering, by a method other
2 than intravenous administration, to an individual in need of said treatment (a) 0.1 mg to 0.8
3 mg of naloxone hydrochloride salt or an equivalent amount of naloxone free base, prodrug,
4 non-hydrochloride salt, or mixture thereof and (b) an amount of pentazocine free base,
5 hydrochloride salt, prodrug, non-hydrochloride salt or mixture thereof that results in greater
6 analgesia than administration of either said naloxone hydrochloride salt or said pentazocine
7 hydrochloride salt alone, provided that 50 mg of pentazocine free base or an equivalent
8 amount of pentazocine hydrochloride salt, non-hydrochloride salt, prodrug, or mixture
9 thereof, is not administered orally for gastro-intestinal uptake with 0.5 mg naloxone free base
10 or equivalent amount of naloxone hydrochloride salt, non-hydrochloride salt, prodrug, or
11 mixture thereof.

1 36. The method of claim 35 wherein the pentazocine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous

3 administration of naloxone hydrochloride salt and 18 to 120 times greater, by weight, of
4 pentazocine hydrochloride salt.

1 37. The method of claim 35 wherein the pentazocine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 10 mg to 50 mg of pentazocine hydrochloride salt.

1 38. The method of claim 35 wherein the pentazocine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 15 mg to 30 mg of pentazocine hydrochloride salt.

1 39. The method of claim 35 wherein administration is nasal.

1 40. The method of claim 39 wherein administration is nasal in the form of
2 a nasal spray or nose drops.

1 41. The method of claim 35 wherein administration is sublingual.

1 42. The method of claim 41 wherein 7.5 to 50 times greater, by weight,
2 pentazocine hydrochloride salt is administered than naloxone hydrochloride salt, or
3 equivalent amounts thereof, respectively, of pentazocine or naloxone free base, non-
4 hydrochloride salt, prodrug, or mixture thereof.

1 43. The method of claim 41 wherein 10 to 30 times greater, by weight,
2 pentazocine hydrochloride salt is administered than naloxone hydrochloride salt, or
3 equivalent amounts thereof, respectively, of pentazocine or naloxone free base, non-
4 hydrochloride salt, prodrug, or mixture thereof.

1 44. The method of claim 41 wherein 30 mg to 100 mg pentazocine
2 hydrochloride salt or equivalent amount of pentazocine free base, non-hydrochloride salt,
3 prodrug or mixture thereof is administered.

1 45. The method of claim 41 wherein 30 mg to 60 mg pentazocine
2 hydrochloride salt or equivalent amount of pentazocine free base, non-hydrochloride salt,
3 prodrug or mixture thereof is administered.

1 46. The method of claim 41 wherein 2 mg to 4 mg naloxone hydrochloride
2 salt or equivalent amount of naloxone free base, non-hydrochloride salt, prodrug or mixture
3 thereof is administered.

1 47. A method of treating pain comprising administering, by a method other
2 than intravenous administration, to an individual in need of said treatment (a) 0.1 mg to 0.8
3 mg of naloxone hydrochloride salt or an equivalent amount of naloxone free base, prodrug,
4 non-hydrochloride salt, or mixture thereof and (b) an amount of butorphanol free base,
5 prodrug, pharmaceutically acceptable salt or mixture thereof that results in greater analgesia
6 than administration of either said nalbuphine hydrochloride salt or said butorphanol alone.

1 48. The method of claim 47 wherein the butorphanol free base, salt,
2 prodrug, or mixture thereof is administered in an amount equivalent to intravenous
3 administration of naloxone hydrochloride salt and 0.3 to 10 times greater, by weight,
4 butorphanol tartrate salt.

1 49. The method of claim 47 wherein naloxone and butorphanol free base,
2 salt, prodrug, or mixture thereof is administered in an amount equivalent to intravenous
3 administration of naloxone hydrochloride salt and 0.5 to 4 times greater, by weight,
4 butorphanol tartrate salt than naloxone hydrochloride salt.

1 50. The method of claim 47 wherein butorphanol free base, salt, prodrug,
2 or mixture thereof is administered in an amount equivalent to intravenous administration of
3 0.2 mg to 2 mg butorphanol tartrate salt.

1 51. The method of claim 47 wherein butorphanol free base, salt, prodrug,
2 or mixture thereof is administered in an amount equivalent to intravenous administration of
3 0.2 mg to 1 mg butorphanol tartrate salt.

1 52. The method of claim 47 wherein the method of administration is
2 mucosal.

1 53. The method of claim 52 wherein administration is nasal.

1 54. The method of claim 53 wherein administration is nasal in the form of
2 a nasal spray or nose drops.

1 55. The method of claim 47 wherein administration is sublingual.

1 56. The method of claim 55 wherein 0.1 to 60 times greater, by weight,
2 butorphanol tartrate salt is administered than naloxone hydrochloride salt, or equivalent
3 amounts thereof, respectively, of butorphanol and/or naloxone free base, other salt, prodrug,
4 or mixture thereof is administered.

1 57. The method of claim 55 wherein 10-30 times greater, by weight,
2 butorphanol tartrate salt is administered than naloxone hydrochloride salt, or equivalent
3 amounts thereof, respectively, of butorphanol and/or naloxone free base, other salt, prodrug,
4 or mixture thereof is administered.

1 58. The method of claim 55 wherein 0.1 mg to 7 mg butorphanol tartrate
2 salt or an equivalent amount of butorphanol free base, other salt, prodrug, or mixture thereof
3 is administered.

1 59. The method of claim 55 wherein 0.5 mg to 6 mg butorphanol tartrate
2 salt or an equivalent amount of butorphanol free base, other salt, prodrug, or mixture thereof
3 is administered.

1 60. The method of claim 55 wherein 0.1 to 1 mg naloxone hydrochloride
2 salt or an equivalent amount of naloxone free base, other salt, prodrug, or mixture thereof is
3 administered.

1 61. A method of treating pain comprising administering intravenously to
2 an individual in need of said treatment (a) 0.1 mg to 0.8 mg of the naloxone hydrochloride
3 salt or an equivalent amount of naloxone free base, prodrug, non-hydrochloride salt, or
4 mixture thereof and (b) an amount of a κ opioid agonist selected from a group consisting of
5 benzomorphan, benzacetamide, phenothiazine, thiazine, and a benzodiazepine, or a
6 pharmaceutically acceptable salt, prodrug, derivative, or mixture thereof, that results in
7 greater analgesia than administration of either said naloxone hydrochloride salt or said κ
8 opioid agonist alone.

1 62. The method of claim 61 wherein the kappa opioid agonist is selected
2 from the group consisting of benzomorphan, benzacetamide, phenothiazine, thiazine, and a

3 benzodiazepine, or a pharmaceutically acceptable salt, prodrug, derivative, or mixture
4 thereof.

1 63. The method of claim 62 wherein the benzomorphan derivative is
2 selected from the group consisting of ketazocine, ethylketazocine, dezocine, bremazocine,
3 and Tifluadom, or pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 64. The method of claim 62 wherein the benzacetamide derivative is
2 selected from the group consisting of U50,488, U69,593, U62,606 (spiradoline), PD 117302,
3 CI-977, DuP 747, ICI 197067, ICI 199441, BRL 52537A, and BRL 52656A, or a
4 pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 65. The method of claim 62 wherein the kappa opioid agonist is the
2 phenothiazine derivative, Rp60180, or a pharmaceutically acceptable salt, prodrug, or
3 mixture thereof.

1 66. The method of claim 62 wherein the kappa receptor agonist is the
2 thiazine derivative, R084760, or a pharmaceutically acceptable salt, prodrug, or mixture
3 thereof.

1 67. A method of treating pain comprising administering to an individual in
2 need of said treatment by a method other than intravenous administration (a) 0.1 mg to 0.8
3 mg of the naloxone hydrochloride salt or an equivalent amount of naloxone free base,
4 prodrug, non-hydrochloride salt, or mixture thereof and (b) an amount of a κ opioid agonist
5 selected from a group consisting of benzomorphan, benzacetamide, phenothiazine, thiazine,
6 and a benzodiazepine, or a pharmaceutically acceptable salt, prodrug, derivative, or mixture
7 thereof, that results in greater analgesia than administration of either said naloxone
8 hydrochloride salt or said κ opioid agonist alone.

1 68. The method of claim 67 wherein the kappa opioid agonist is selected
2 from the group consisting of benzomorphan, benzacetamide, phenothiazine, thiazine, and a
3 benzodiazepine, or a pharmaceutically acceptable salt, prodrug, derivative, or mixture
4 thereof.

1 69. The method of claim 68 wherein the benzomorphan derivative is
2 selected from the group consisting of ketazocine, ethylketazocine, dezocine, bremazocine,
3 and Tifluadom, or pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 70. The method of claim 68 wherein the benzacetamide derivative is
2 selected from the group consisting of U50,488, U69,593, U62,606 (spiradoline), PD 117302,
3 CI-977, DuP 747, ICI 197067, ICI 199441, BRL 52537A, and BRL 52656A, or a
4 pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 71. The method of claim 68 wherein the kappa opioid agonist is the
2 phenothiazine derivative, Rp60180, or a pharmaceutically acceptable salt, prodrug, or
3 mixture thereof.

1 72. The method of claim 68 wherein the kappa receptor agonist is the
2 thiazine derivative, R084760, or a pharmaceutically acceptable salt, prodrug, or mixture
3 thereof.

1 73. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg of
2 naloxone hydrochloride salt or an equivalent amount of naloxone freebase, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) an amount of nalbuphine free base, salt, prodrug,
4 or mixture thereof that results in greater analgesia than administration of said nalbuphine or
5 said naloxone alone; and (c) a pharmaceutically acceptable carrier, said pharmaceutical
6 composition being formulated for intravenous administration, provided that the composition
7 does not comprise 5 mg nalbuphine free base with 0.4 mg naloxone free base.

1 74. The composition of claim 73 wherein the amount of nalbuphine
2 hydrochloride salt is 6.25 to 49 times greater, by weight, than the amount of naloxone
3 hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug, non-chloride
4 salt, or mixture thereof.

1 75. The composition of claim 73 wherein the amount of nalbuphine
2 hydrochloride salt is 8 to 30 times greater, by weight, than the amount of naloxone
3 hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug, non-chloride
4 salt, or mixture thereof.

1 76. The composition of claim 73 wherein the amount of nalbuphine
2 hydrochloride salt is 10 to 20 times greater, by weight, than the amount of naloxone
3 hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug, non-chloride
4 salt, or mixture thereof.

1 77. The composition of claim 73 wherein the amount of nalbuphine
2 hydrochloride salt is 1 mg to 10 mg or an equivalent amount of nalbuphine free base,
3 prodrug, non-chloride salt, or mixture thereof.

1 78. The composition of claim 73 wherein the amount of nalbuphine
2 hydrochloride salt is 3 mg to 8 mg or an equivalent amount of nalbuphine free base, prodrug,
3 non-chloride salt, or mixture thereof.

1 79. The composition of claim 73 wherein the amount of nalbuphine
2 hydrochloride salt is 1 mg to 6 mg or an equivalent amount of nalbuphine free base, prodrug,
3 non-chloride salt, or mixture thereof.

1 80. The composition of claim 73 comprising 0.5 mg to 0.8 mg naloxone
2 hydrochloride salt or an equivalent amount of naloxone free base, prodrug, non-chloride salt,
3 or mixture thereof.

1 81. The composition of claim 73 comprising 0.1 mg to 0.5 mg naloxone
2 hydrochloride salt or an equivalent amount of naloxone free base, prodrug, non-chloride salt,
3 or mixture thereof is administered, provided that the composition does not comprise 5 mg
4 nalbuphine free base with 0.4 mg naloxone free base.

1 82. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg of
2 naloxone hydrochloride salt or an equivalent amount of naloxone freebase, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) an amount of pentazocine free base, salt, prodrug,
4 or mixture thereof that results in greater analgesia than administration of said pentazocine or
5 said naloxone hydrochloride salt alone; and (c) a pharmaceutically acceptable carrier, said
6 pharmaceutical composition being formulated for intravenous administration, provided that
7 the composition does not comprise 60 mg of pentazocine with 0.4 mg naloxone.

1 83. The composition of claim 82 comprising pentazocine hydrochloride
2 salt is administered in an amount 18 to 120 times greater, by weight, than the amount of

3 naloxone hydrochloride salt or an equivalent amount of pentazocine free base, prodrug, non-
4 hydrochloride salt, or mixture thereof, provided that the composition does not comprise 60
5 mg of pentazocine with 0.4 mg naloxone.

1 84. The composition of claim 82 comprising pentazocine hydrochloride
2 salt is administered in an amount 18 to 50 times greater, by weight, than the amount of
3 naloxone hydrochloride salt or an equivalent amount of pentazocine free base, prodrug, non-
4 hydrochloride salt, or mixture thereof, provided that the composition does not comprise 60
5 mg of pentazocine with 0.4 mg naloxone.

1 85. The composition of claim 82 comprising 3 mg to 50 mg pentazocine
2 hydrochloride salt or an equivalent amount of pentazocine free base, prodrug, hydrochloride
3 salt, or mixture thereof.

1 86. The composition of claim 82 comprising 3 mg to 30 mg pentazocine
2 hydrochloride salt or an equivalent amount of pentazocine free base, prodrug, hydrochloride
3 salt, or mixture thereof.

1 87. The composition of claim 82 comprising 10 mg to 20 mg pentazocine
2 hydrochloride salt or an equivalent amount of pentazocine free base, prodrug, hydrochloride
3 salt, or mixture thereof.

1 88. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg of
2 naloxone hydrochloride salt or an equivalent amount of naloxone freebase, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) an amount of butorphanol free base, salt, prodrug,
4 or mixture thereof that results in greater analgesia than administration of said butorphanol or
5 said naloxone alone; and (c) a pharmaceutically acceptable carrier, said pharmaceutical
6 composition being formulated for intravenous administration.

1 89. The composition of claim 88 comprising 0.3 to 10 times greater, by
2 weight, butorphanol tartrate salt than naloxone hydrochloride salt, or equivalent amounts of,
3 respectively, butorphanol free base, non-tartrate salt, prodrug, or mixture thereof and
4 naloxone free base, non-hydrochloride salt, prodrug, or mixture thereof.

1 90. The composition of claim 88 comprising 0.3 to 6 times greater, by
2 weight, butorphanol tartrate salt than naloxone hydrochloride salt, or equivalent amounts of,

3 respectively, butorphanol free base, non-tartrate salt, prodrug, or mixture thereof and
4 naloxone free base, non-hydrochloride salt, prodrug, or mixture thereof.

1 91. The composition of claim 88 comprising 0.2 mg to 2 mg butorphanol
2 tartrate salt or an equivalent amount of butorphanol free base, non-tartrate salt, prodrug, or
3 mixture thereof.

1 92. The composition of claim 88 comprising 0.2 mg to 1.2 mg butorphanol
2 tartrate salt or an equivalent amount of butorphanol free base, non-tartrate salt, prodrug, or
3 mixture thereof.

1 93. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg of
2 naloxone hydrochloride salt or an equivalent amount of naloxone freebase, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) an amount of a κ opioid agonist selected from the
4 group consisting of benzomorphan, benzacetamide, phenothiazine, thiazine, and a
5 benzodiazepine, or a pharmaceutically acceptable salt, prodrug, derivative, or mixture
6 thereof, that results in greater analgesia than administration of said κ -opioid agonist or said
7 naloxone alone; and (c) a pharmaceutically acceptable carrier, said pharmaceutical
8 composition being formulated for intravenous administration.

1 94. The composition of claim 93 wherein the kappa opioid agonist is
2 selected from the group consisting of benzomorphan, benzacetamide, phenothiazine, thiazine,
3 and a benzodiazepine, or a pharmaceutically acceptable salt, prodrug, derivative, or mixture
4 thereof.

1 95. The composition of claim 93 wherein the benzodiazepine derivative is
2 selected from the group consisting of ketazocine, ethylketazocine, dezocine, bremazocine,
3 and Tifluadom, or pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 96. The composition of claim 93 wherein the benzacetamide derivative is
2 selected from the group consisting of U50,488, U69,593, U62,606 (spiradoline), PD 117302,
3 CI-977, DuP 747, ICI 197067, ICI 199441, BRL 52537A, and BRL 52656A, or a
4 pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 97. The composition of claim 93 wherein the kappa opioid agonist is the
2 phenothiazine derivative, Rp60180, or a pharmaceutically acceptable salt, prodrug, or
3 mixture thereof.

1 98. The composition of claim 93 wherein the kappa receptor agonist is the
2 thiazine derivative, R084760, or a pharmaceutically acceptable salt, prodrug, or mixture
3 thereof.

1 99. The composition of claim 93 wherein the kappa opioid agonist is
2 nalbuphine or a hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof.

1 100. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg of an
2 naloxone hydrochloride salt or an equivalent amount of naloxone freebase, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) an amount of nalbuphine free base, salt, prodrug,
4 or mixture thereof that results in greater analgesia than administration of the said nalbuphine
5 or said naloxone alone; and (c) a pharmaceutically acceptable carrier, said pharmaceutical
6 composition being formulated for administration other than intravenous administration.

1 101. The composition claim 100 comprising nalbuphine free base, salt,
2 prodrug, or mixture thereof, in an amount equivalent to intravenous administration of the
3 naloxone hydrochloride salt and 6.25 to 30 times greater in weight of nalbuphine
4 hydrochloride salt than the naloxone hydrochloride salt.

1 102. The composition claim 100 comprising nalbuphine free base, salt,
2 prodrug, or mixture thereof, in an amount equivalent to intravenous administration of the
3 naloxone hydrochloride salt and 10 to 20 times greater in weight of nalbuphine hydrochloride
4 salt than the naloxone hydrochloride salt.

1 103. The composition claim 100 comprising nalbuphine free base, salt,
2 prodrug, or mixture thereof, in an amount equivalent to intravenous administration of 1 mg to
3 10 mg of nalbuphine hydrochloride salt.

1 104. The composition claim 100 comprising nalbuphine free base, salt,
2 prodrug, or mixture thereof, in an amount equivalent to intravenous administration of 1 mg to
3 6 mg of nalbuphine hydrochloride salt.

1 105. The composition of any of the claims 100 to 104 wherein the
2 composition is formulated for mucosal administration.

1 106. The composition of claim 105 wherein the composition is formulated
2 for nasal administration.

1 107. The composition of claim 105 wherein the composition is formulated
2 for nasal administration in the form of a nasal spray or nose drops.

1 108. The composition of claims 100 wherein the composition is formulated
2 for sublingual administration.

1 109. The composition of claim 108 comprising 1 to 60 times greater, by
2 weight, nalbuphine hydrochloride salt than naloxone hydrochloride salt, or equivalent
3 amounts thereof, respectively, of nalbuphine free base, non-hydrochloride salt, prodrug, or
4 mixture thereof and naloxone free base, non-hydrochloride salt, prodrug, and mixture thereof.

1 110. The composition of claim 108 comprising 1 to 30 times greater, by
2 weight, nalbuphine hydrochloride salt is administered than naloxone hydrochloride salt, or
3 equivalent amounts thereof, respectively, of nalbuphine free base, non-hydrochloride salt,
4 prodrug, or mixture thereof and naloxone free base, non-hydrochloride salt, prodrug, and
5 mixture thereof.

1 111. The composition of claim 108 comprising 5 mg to 65 mg nalbuphine
2 hydrochloride salt or an equivalent amount of nalbuphine free base, non-hydrochloride salt,
3 prodrug, or mixture thereof.

1 112. The composition of claim 108 comprising 7.5 mg to 30 mg nalbuphine
2 hydrochloride salt or an equivalent amount of nalbuphine free base, non-hydrochloride salt,
3 prodrug, or mixture thereof.

1 113. The composition of any claims 108 to 112 comprising 0.4 mg to 4 mg
2 naloxone hydrochloride salt or an equivalent amount of naloxone free base, non-
3 hydrochloride salt, prodrug, or mixture thereof.

1 114. The composition of any claims 108 to 112 comprising 0.4 mg to 2.5
2 mg naloxone hydrochloride salt or an equivalent amount of naloxone free base, non-
3 hydrochloride salt, prodrug, or mixture thereof.

1 115. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg of
2 naloxone hydrochloride salt or an equivalent amount of naloxone freebase, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) an amount of pentazocine free base, salt, prodrug,
4 or mixture thereof that results in greater analgesia than administration of said pentazocine or
5 said naloxone alone; and (c) a pharmaceutically acceptable carrier, said pharmaceutical
6 composition being formulated for administration other than intravenous administration,
7 provided that the composition formulated for oral administration does not comprise 50 mg
8 pentazocine hydrochloride salt with 0.5 mg naloxone hydrochloride salt.

1 116. The composition of claim 115 comprising an amount of pentazocine
2 free base, salt, prodrug, or mixture thereof, equivalent to intravenous administration of the
3 opioid antagonist hydrochloride salt and 18 to 120 times greater, by weight, of pentazocine
4 hydrochloride salt.

1 117. The composition of claim 115 comprising an amount of pentazocine
2 free base, salt, prodrug, or mixture thereof, equivalent to intravenous administration of 10
3 mg to 50 mg of pentazocine hydrochloride salt.

1 118. The composition of claim 115 comprising an amount of pentazocine
2 free base, salt, prodrug, or mixture thereof, equivalent to intravenous administration of 15 mg
3 to 30 mg of pentazocine hydrochloride salt.

1 119. The composition of claim 115 wherein the composition is formulated
2 for mucosal administration.

1 120. The composition of claim 119 wherein the composition is formulated
2 for nasal administration.

1 121. The composition of claim 120 wherein the composition is formulated
2 for nasal administration in the form of a nasal spray or nose drops.

1 122. The composition of claim 115 wherein the composition is formulated
2 for sublingual administration.

1 123. The composition of claim 122 comprising 7.5 to 50 times greater, by
2 weight, pentazocine hydrochloride salt than naloxone hydrochloride salt, or equivalent
3 amounts thereof, respectively, of pentazocine or naloxone free base, non-hydrochloride salt,
4 prodrug, or mixture thereof.

1 124. The composition of claim 122 comprising 10 to 30 times greater, by
2 weight, pentazocine hydrochloride salt than naloxone hydrochloride salt, or equivalent
3 amounts thereof, respectively, of pentazocine or naloxone free base, non-hydrochloride salt,
4 prodrug, or mixture thereof.

1 125. The composition of claim 122 comprising 30 mg to 100 mg
2 pentazocine hydrochloride salt or equivalent amount of pentazocine free base, non-
3 hydrochloride salt, prodrug or mixture thereof.

1 126. The composition of claim 122 comprising 30 mg to 60 mg pentazocine
2 hydrochloride salt or equivalent amount of pentazocine free base, non-hydrochloride salt,
3 prodrug or mixture thereof.

1 127. The composition of claim 122 comprising 2 mg to 4 mg naloxone
2 hydrochloride salt or equivalent amount of naloxone free base, non-hydrochloride salt,
3 prodrug or mixture thereof.

1 128. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg
2 naloxone hydrochloride salt or an equivalent amount of naloxone freebase, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) an amount of butorphanol free base, salt, prodrug,
4 or mixture thereof that results in greater analgesia than administration of said butorphanol or
5 said naloxone alone; and (c) a pharmaceutically acceptable carrier, said pharmaceutical
6 composition being formulated for administration other than intravenous administration.

1 129. The composition of claim 128 comprising butorphanol free base, salt,
2 prodrug, or mixture thereof in an amount equivalent to intravenous administration of
3 naloxone hydrochloride salt and 0.3 to 10 times greater, by weight, butorphanol tartrate salt.

1 130. The composition of claim 128 comprising butorphanol free base, salt,
2 prodrug, or mixture thereof in an amount equivalent to intravenous administration of
3 naloxone hydrochloride salt and 0.3 to 6 times greater, by weight, butorphanol tartrate salt.

1 131. The composition of claim 128 comprising butorphanol free base, salt,
2 prodrug, or mixture thereof in an amount equivalent to intravenous administration of 0.2 mg
3 to 2 mg butorphanol tartrate salt.

1 132. The composition of claim 128 comprising butorphanol free base, salt,
2 prodrug, or mixture thereof in an amount equivalent to intravenous administration of 0.2 mg
3 to 1 mg butorphanol tartrate salt.

1 133. The compositions of claim 128 wherein the composition is formulated
2 for mucosal administration.

1 134. The composition of claim 133 wherein the composition is formulated
2 for nasal administration.

1 135. The composition of claim 134 wherein the composition is formulated
2 for nasal administration the form of a nasal spray or nose drops.

1 136. The composition of claim 128 wherein the composition is formulated
2 for sublingual administration.

1 137. The composition of claim 136 comprising 0.1 to 60 times greater, by
2 weight, butorphanol tartrate salt than naloxone hydrochloride salt, or equivalent amounts
3 thereof, respectively, of butorphanol and/or naloxone free base, other salt, prodrug, or
4 mixture thereof.

1 138. The composition of claim 136 comprising 10-30 times greater, by
2 weight, butorphanol tartrate salt is administered than naloxone hydrochloride salt, or
3 equivalent amounts thereof, respectively, of butorphanol and/or naloxone free base, other
4 salt, prodrug, or mixture thereof.

1 139. The composition of claim 138 comprising 0.1 mg to 7 mg butorphanol
2 tartrate salt or an equivalent amount of butorphanol free base, other salt, prodrug, or mixture
3 thereof.

1 140. The composition of claim 138 comprising 0.5 mg to 6 mg butorphanol
2 tartrate salt or an equivalent amount of butorphanol free base, other salt, prodrug, or mixture
3 thereof.

1 141. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg of
2 naloxone hydrochloride salt or an equivalent amount of naloxone freebase, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) an amount of a κ opioid agonist selected from the
4 group consisting of benzomorphan, benzacetamide, phenothiazine, thiazine, and a
5 benzodiazepine, or a pharmaceutically acceptable salt, prodrug, derivative, or mixture
6 thereof, that results in greater analgesia than administration of said κ opioid agonist or said
7 naloxone alone; and (c) a pharmaceutically acceptable carrier, said pharmaceutical
8 composition being formulated for intravenous administration.

1 142. The method of claim 141 wherein the kappa opioid agonist is selected
2 from the group consisting of benzomorphan, benzacetamide, phenothiazine, thiazine, and a
3 benzodiazepine, or a pharmaceutically acceptable salt, prodrug, derivative, or mixture
4 thereof.

1 143. The composition of claim 142 wherein the benzodiazepine derivative
2 is selected from the group consisting of ketazocine, ethylketazocine, dezocine, bremazocine,
3 and Tifluadom, or pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 144. The composition of claim 142 wherein the benzacetamide derivative is
2 selected from the group consisting of U50,488, U69,593, U62,606 (spiradoline), PD 117302,
3 CI-977, DuP 747, ICI 197067, ICI 199441, BRL 52537A, and BRL 52656A, or a
4 pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 145. The composition of claim 142 wherein the kappa opioid agonist is the
2 phenothiazine derivative, Rp60180, or a pharmaceutically acceptable salt, prodrug, or
3 mixture thereof.

1 146. The composition of claim 142 wherein the kappa receptor agonist is
2 the thiazine derivative, R084760, or a pharmaceutically acceptable salt, prodrug, or mixture
3 thereof.

1 147. The composition of claim 142 wherein the kappa opioid agonist is
2 nalbuphine or a hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof.

1 148. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg of
2 naloxone hydrochloride salt or an equivalent amount of naloxone freebase, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) an amount of a κ opioid agonist selected from the
4 group consisting of benzomorphan, benzacetamide, phenothiazine, thiazine, and a
5 benzodiazepine, or a pharmaceutically acceptable salt, prodrug, derivative, or mixture
6 thereof, that results in greater analgesia than administration of said κ opioid agonist or said
7 naloxone alone; and (c) a pharmaceutically acceptable carrier, said pharmaceutical
8 composition being formulated for administration by a method other than intravenous
9 administration.

1 149. The method of claim 148 wherein the kappa opioid agonist is selected
2 from the group consisting of benzomorphan, benzacetamide, phenothiazine, thiazine, and a
3 benzodiazepine, or a pharmaceutically acceptable salt, prodrug, derivative, or mixture
4 thereof.

1 150. The composition of claim 149 wherein the benzodiazepine derivative
2 is selected from the group consisting of ketazocine, ethylketazocine, dezocine, bremazocine,
3 and Tifluadom, or pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 151. The composition of claim 149 wherein the benzacetamide derivative is
2 selected from the group consisting of U50,488, U69,593, U62,606 (spiradoline), PD 117302,
3 CI-977, DuP 747, ICI 197067, ICI 199441, BRL 52537A, and BRL 52656A, or a
4 pharmaceutically acceptable salt, prodrug, or mixture thereof.

1 152. The composition of claim 149 wherein the kappa opioid agonist is the
2 phenothiazine derivative, Rp60180, or a pharmaceutically acceptable salt, prodrug, or
3 mixture thereof.

1 153. The composition of claim 149 wherein the kappa receptor agonist is
2 the thiazine derivative, R084760, or a pharmaceutically acceptable salt, prodrug, or mixture
3 thereof.

1 154. A method of treating pain comprising mucosally administering to an
2 individual in need of said treatment (a) 0.1 mg to 0.8 mg of a hydrochloride salt of an opioid
3 antagonist or an equivalent amount of opioid antagonist free base, prodrug, non-
4 hydrochloride salt, or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone,
5 methylnaltrexone, nalmefene, nalorphine, levalorphan, oxylorphan or cyprenorphine, and (b)
6 an amount of nalbuphine free base, hydrochloride salt, prodrug, non-hydrochloride salt or
7 mixture thereof that results in greater analgesia than administration of either said opioid
8 antagonist hydrochloride salt or said nalbuphine alone.

1 155. A method according to claim 154 wherein the opioid antagonist is a
2 salt of naloxone, naltrexone, methylnaltrexone, nalmefene, nalorphine, levalorphan,
3 oxylorphan, or cyprenorphine.

1 156. A method according to claim 154 wherein the opioid antagonist is
2 naloxone or a salt or prodrug of naloxone.

1 157. A method according to claim 154 wherein an opioid antagonist
2 hydrochloride salt is administered and the amount of nalbuphine hydrochloride salt
3 administered is 6.25 to 49 times greater, by weight, than the amount of opioid antagonist
4 hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug, non-chloride
5 salt, or mixture thereof, is administered.

1 158. A method according to claim 154 wherein an opioid antagonist
2 hydrochloride salt is administered and the amount of nalbuphine hydrochloride salt
3 administered is 10 to 15 times greater, by weight, than the amount of naloxone hydrochloride
4 salt, or an equivalent amount of nalbuphine free base, prodrug, non-chloride salt, or mixture
5 thereof, is administered.

1 159. A method according to claim 154 wherein an opioid antagonist
2 hydrochloride salt is administered and the amount of nalbuphine hydrochloride salt
3 administered is 12.5 times greater, by weight, than the amount of naloxone hydrochloride
4 salt, or an equivalent amount of nalbuphine free base, prodrug, non-chloride salt, or mixture
5 thereof, is administered.

1 160. A method according to claim 154 wherein 2 mg to 10 mg of
2 nalbuphine hydrochloride salt is administered, or an equivalent amount of nalbuphine free
3 base, prodrug, non-chloride salt, or mixture thereof, is administered.

1 161. A method according to claim 154 wherein 0.1 mg to 0.8 mg of
2 naloxone hydrochloride salt is administered, or an equivalent amount of naloxone free base,
3 prodrug, non-chloride salt, or mixture thereof, is administered.

1 162. A method according to claim 154 wherein 2 mg to 5 mg of nalbuphine
2 hydrochloride salt is administered, or an equivalent amount of nalbuphine free base, prodrug,
3 non-chloride salt, or mixture thereof, is administered.

1 163. A method according to claim 154 wherein 0.4 mg of naloxone
2 hydrochloride and 5 mg of nalbuphine hydrochloride are administered.

1 164. A method according to claim 154 wherein 0.2 mg of naloxone
2 hydrochloride and 2.5 mg of nalbuphine hydrochloride are administered.

1 165. A method according to claim 154 wherein 0.8 mg of naloxone
2 hydrochloride and 10 mg of nalbuphine hydrochloride are administered.

1 166. A method according to claim 154 wherein the ingredients are
2 administered intranasally.

1 167. A method according to claim 154 wherein the ingredients are
2 administered by pulmonary administration.

1 168. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) 0.1 mg to 0.8 mg of a hydrochloride salt of an opioid antagonist or
3 an equivalent amount of opioid antagonist free base, prodrug, non-hydrochloride salt, or
4 mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone,
5 nalmeфene, nalorphine, levalorphan, oxylorphan or cyprenorphine, and (b) an amount of a
6 free base, hydrochloride salt, prodrug, non-hydrochloride salt or mixture thereof of a kappa-
7 opioid, that results in greater analgesia than administration of either said opioid antagonist
8 hydrochloride salt or said kappa-opioid, wherein the kappa-opioid is pentazocine,
9 butorphanol, ketazocine, ethylketazocine, dezocine, bremazocine, a benzacetamide

10 derivative, a phenothiazine derivative, a thiazine derivative, or a benzodiazepine derivative,
11 provided that 60 mg of pentazocine free base or an equivalent amount of pentazocine
12 hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof, is not administered
13 with 0.4 mg naloxone free base or equivalent amount of naloxone hydrochloride salt, non-
14 hydrochloride salt, prodrug, or mixture thereof.

1 169. A method according to claim 168 wherein the kappa-opioid is
2 pentazocine and the opioid antagonist is naloxone.

1 170. A method according to claim 169 wherein pentazocine hydrochloride
2 salt is administered in an amount 18 to 30 times greater, by weight, than the amount of
3 naloxone hydrochloride salt, or an equivalent amount of pentazocine free base, prodrug, non-
4 hydrochloride salt, or mixture thereof is administered.

1 171. A method according to claim 168 wherein the kappa-opioid is
2 butorphanol and the opioid antagonist is naloxone.

1 172. A method according to claim 175 wherein 0.3 to 10 times greater, by
2 weight, butorphanol tartrate salt than naloxone hydrochloride salt is administered, or
3 equivalent amount of butorphanol free base, non-tartrate salt, prodrug, or mixture thereof
4 and/or naloxone free base, non-hydrochloride salt, prodrug, or mixture thereof is
5 administered.

1 173. A method according to claim 168 wherein 0.1 to 0.8 mg naloxone
2 hydrochloride salt or an equivalent amount of naloxone free base, non-hydrochloride salt,
3 prodrug, or mixture thereof is administered

1 174. A method according to claim 168 wherein the ingredients are
2 administered intravenously.

1 175. A method according to any of claim 168 wherein the ingredients are
2 administered mucosally.

1 176. A method according to claim 168 wherein the ingredients are
2 administered intranasally.

1 177. A method according to claim 168 wherein the ingredients are
2 administered by pulmonary administration.

1 178. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) from 0.1 to 0.8 mg of a hydrochloride salt of naloxone or an
3 equivalent amount of naloxone free base, prodrug, non-hydrochloride salt, or mixture thereof;
4 and (b) from 1 to 2.5 mg of nalbuphine hydrochloride, or an equivalent amount of nalbuphine
5 free base, prodrug, non-hydrochloride salt or mixture thereof.

1 179. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) from 0.1 to 0.8 mg of a hydrochloride salt of naloxone or an
3 equivalent amount of naloxone free base, prodrug, non-hydrochloride salt, or mixture thereof;
4 and (b) from 8.5 to 10 mg of nalbuphine hydrochloride, or an equivalent amount of
5 nalbuphine free base, prodrug, non-hydrochloride salt or mixture thereof.

1 180. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) 0.1 mg of a hydrochloride salt of naloxone or an equivalent amount
3 of naloxone free base, prodrug, non-hydrochloride salt, or mixture thereof; and (b) 1.25 mg of
4 nalbuphine hydrochloride, or an equivalent amount of nalbuphine free base, prodrug, non-
5 hydrochloride salt or mixture thereof.

1 181. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) 0.2 mg of a hydrochloride salt of naloxone or an equivalent amount
3 of naloxone free base, prodrug, non-hydrochloride salt, or mixture thereof; and (b) 2.5 mg of
4 nalbuphine hydrochloride, or an equivalent amount of nalbuphine free base, prodrug, non-
5 hydrochloride salt or mixture thereof.

1 182. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) 0.8 mg of a hydrochloride salt of naloxone or an equivalent amount
3 of naloxone free base, prodrug, non-hydrochloride salt, or mixture thereof; and (b) 10 mg of
4 nalbuphine hydrochloride, or an equivalent amount of nalbuphine free base, prodrug, non-
5 hydrochloride salt or mixture thereof.

1 183. A method according to claim 178 wherein the ingredients are
2 administered intravenously.

- 1 184. A method according to claim 178 wherein the ingredients are
2 administered mucosally.
- 1 185. A method according to claim 178 wherein the ingredients are
2 administered intranasally.
- 1 186. A method according to claim 178 wherein the ingredients are
2 administered by pulmonary administration.
- 1 187. A method according to claim 154 wherein the pain is neuropathic pain.
- 1 188. A method according to claim 154 wherein the pain is inflammatory
2 pain.
- 1 189. A method according to claim 154 wherein the pain is acute pain.
- 1 190. A method according to claim 154 wherein the pain is traumatic pain.
- 1 191. A method according to claim 154 wherein the pain is post-procedural
2 pain.
- 1 192. A method according to claim 154 wherein the pain is infection-related
2 pain.
- 1 193. A pharmaceutical composition comprising (a) 0.1 mg to 0.8 mg of a
2 hydrochloride salt of an opioid antagonist or an equivalent amount of opioid antagonist free
3 base, prodrug, non-hydrochloride salt, or mixture thereof, wherein said opioid antagonist is
4 naloxone, naltrexone, methylnaltrexone, nalmefene, nalorphine, levalorphan, oxylorphan or
5 cyprenorphine; (b) an amount of nalbuphine free base, nalbuphine salt, nalbuphine prodrug,
6 or mixture thereof that results in greater analgesia than administration of the nalbuphine
7 ingredient or the opioid antagonist ingredient alone; and (c) a pharmaceutically acceptable
8 carrier, said pharmaceutical composition being formulated for mucosal administration.
- 1 194. A composition according to claim 193 wherein the opioid antagonist is
2 a salt of naloxone, naltrexone, methylnaltrexone, nalmefene, nalorphine, levalorphan,
3 oxylorphan, or cyprenorphine.

1 195. A composition according to claim 193 wherein the opioid antagonist is
2 naloxone or a salt or prodrug of naloxone.

1 196. A composition according to claim 193 comprising nalbuphine
2 hydrochloride, the amount of nalbuphine hydrochloride salt being 6.25 to 49 times greater, by
3 weight, than the amount of opioid antagonist hydrochloride salt, or an equivalent amount of
4 nalbuphine free base, prodrug, non-hydrochloride salt, or mixture thereof.

1 197. A composition according to claim 193 comprising nalbuphine
2 hydrochloride, the amount of nalbuphine hydrochloride salt being 10 to 15 times greater, by
3 weight, than the amount of naloxone hydrochloride salt, or an equivalent amount of
4 nalbuphine free base, prodrug, non-hydrochloride salt, or mixture thereof.

1 198. A composition according to claim 193 comprising nalbuphine
2 hydrochloride, the amount of nalbuphine hydrochloride salt being 12.5 times greater, by
3 weight, than the amount of naloxone hydrochloride salt, or an equivalent amount of
4 nalbuphine free base, prodrug, non-hydrochloride salt, or mixture thereof.

1 199. A composition according to claim 193 comprising 1.25 mg to 10 mg of
2 nalbuphine hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug,
3 non-hydrochloride salt, or mixture thereof.

1 200. A composition according to claim 193 comprising 0.1 mg to 0.8 mg of
2 naloxone hydrochloride salt or an equivalent amount of naloxone free base, prodrug, non-
3 hydrochloride salt, or mixture thereof.

1 201. A composition according to claim 193 comprising 1 mg to 2.5 mg of
2 nalbuphine hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug,
3 non-chloride salt, or mixture thereof and 0.1 to 0.8 naloxone hydrochloride salt or an
4 equivalent amount of naloxone free base, prodrug, non-hydrochloride salt or mixture thereof.

1 202. A composition according to claim 193 comprising 8.5 mg to 10 mg of
2 nalbuphine hydrochloride salt, or an equivalent amount of nalbuphine free base, prodrug,
3 non-chloride salt, or mixture thereof and 0.1 to 0.8 naloxone hydrochloride salt or an
4 equivalent amount of naloxone free base, prodrug, non-hydrochloride salt or mixture thereof.

1 203. A composition according to claim 193 comprising 0.4 mg of naloxone
2 hydrochloride and 5 mg of nalbuphine hydrochloride.

1 204. A composition according to claim 193 comprising 0.125 mg of
2 naloxone hydrochloride and 2.5 mg of nalbuphine hydrochloride.

1 205. A composition according to claim 193 comprising 0.2 mg of naloxone
2 hydrochloride and 2.5 mg of nalbuphine hydrochloride.

1 206. A composition according to claim 193 comprising 0.8 mg of naloxone
2 hydrochloride and 10 mg of nalbuphine hydrochloride.

1 207. A composition according to claim 193 formulated for intranasal
2 administration.

1 208. A composition according to claim 193 formulated for pulmonary
2 administration.

1 209. A composition for treating pain comprising (a) 0.1 mg to 0.8 mg of a
2 hydrochloride salt of an opioid antagonist or an equivalent amount of opioid antagonist free
3 base, prodrug, non-hydrochloride salt, or mixture thereof, wherein said opioid antagonist is
4 naloxone, naltrexone, methylnaltrexone, nalmefene, nalorphine, levalorphan, oxylorphan or
5 cyprenorphine; (b) an amount of a free base, hydrochloride salt, prodrug, non-hydrochloride
6 salt or mixture thereof of a kappa- opioid, that results in greater analgesia than administration
7 of either said opioid antagonist hydrochloride salt or said kappa-opioid, wherein the kappa-
8 opioid is pentazocine, butorphanol, ketazocine, ethylketazocine, dezocine,bremazocine, a
9 benzacetamide derivative, a phenothiazine derivative, a thiazine derivative, or a
10 benzodiazepine derivative; and (c) a pharmaceutically acceptable carrier; provided that the
11 composition does not comprise 60 mg of pentazocine free base or an equivalent amount of
12 pentazocine hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof and 0.4
13 mg naloxone free base or equivalent amount of naloxone hydrochloride salt, non-
14 hydrochloride salt, prodrug, or mixture thereof.

1 210. A composition according to claim 209 wherein the kappa-opioid is
2 pentazocine and the opioid antagonist is naloxone.

1 211. A composition according to claim 210 comprising pentazocine
2 hydrochloride salt in an amount 18 to 30 times greater, by weight, than the amount of
3 naloxone hydrochloride salt, or an equivalent amount of pentazocine free base, prodrug, non-
4 hydrochloride salt, or mixture thereof.

1 212. A composition according to claim 209 wherein the kappa-opioid is
2 butorphanol and the opioid antagonist is naloxone.

1 213. A composition according to claim 212 comprising 0.3 to 10 times
2 greater, by weight, butorphanol tartrate salt than naloxone hydrochloride salt, or equivalent
3 amount of butorphanol free base, non-tartrate salt, prodrug, or mixture thereof and/or
4 naloxone free base, non-hydrochloride salt, prodrug, or mixture thereof.

1 214. A composition according to claim 212 comprising 0.1 to 0.8 mg
2 naloxone hydrochloride salt or an equivalent amount of naloxone free base, non-
3 hydrochloride salt, prodrug, or mixture thereof.

1 215. A composition according to claim 209 formulated for intravenous
2 administration.

1 216. A composition according to claim 209 formulated for mucosal
2 administration.

1 217. A composition according to claim 209 formulated for intranasal
2 administration.

1 218. A composition according to claim 209 formulated for pulmonary
2 administration.

1 219. A composition for treating pain comprising (a) 0.1 to 0.8 mg of a
2 hydrochloride salt of naloxone or an equivalent amount of naloxone free base, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) 1-2.5 mg of nalbuphine hydrochloride, or an
4 equivalent amount of nalbuphine free base, prodrug, non-hydrochloride salt or mixture
5 thereof; and (c) a pharmaceutically acceptable carrier.

1 220. A composition for treating pain comprising (a) 0.1 to 0.8 mg of a
2 hydrochloride salt of naloxone or an equivalent amount of naloxone free base, prodrug, non-

3 hydrochloride salt, or mixture thereof; (b) 8.5 to 10 mg of nalbuphine hydrochloride, or an
4 equivalent amount of nalbuphine free base, prodrug, non-hydrochloride salt or mixture
5 thereof; and (c) a pharmaceutically acceptable carrier.

1 221. A composition for treating pain comprising (a) 0.1 mg of a
2 hydrochloride salt of naloxone or an equivalent amount of naloxone free base, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) 1.25 mg of nalbuphine hydrochloride, or an
4 equivalent amount of nalbuphine free base, prodrug, non-hydrochloride salt or mixture
5 thereof; and (c) a pharmaceutically acceptable carrier.

1 222. A composition for treating pain comprising (a) 0.2 mg of a
2 hydrochloride salt of naloxone or an equivalent amount of naloxone free base, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) 2.5 mg of nalbuphine hydrochloride, or an
4 equivalent amount of nalbuphine free base, prodrug, non-hydrochloride salt or mixture
5 thereof; and (c) a pharmaceutically acceptable carrier.

1 223. A composition for treating pain comprising (a) 0.8 mg of a
2 hydrochloride salt of naloxone or an equivalent amount of naloxone free base, prodrug, non-
3 hydrochloride salt, or mixture thereof; (b) 10 mg of nalbuphine hydrochloride, or an
4 equivalent amount of nalbuphine free base, prodrug, non-hydrochloride salt or mixture
5 thereof; and (c) a pharmaceutically acceptable carrier.

1 224. A composition according to claim 193 formulated for treatment of
2 neuropathic pain.

1 225. A composition according to claim 193 formulated for treatment of
2 inflammatory pain.

1 226. A composition according to claim 193 formulated for treatment of
2 acute pain.

1 227. A composition according to claim 193 formulated for treatment of
2 traumatic pain.

1 228. A composition according to claim 193 formulated for treatment of
2 post-procedural pain.

1 229. A composition according to claim 193 formulated for treatment of
2 infection-related pain.

1 230. A method of treating pain comprising mucosally administering to an
2 individual in need of said treatment (a) an amount of an opioid antagonist free base, prodrug,
3 salt, or mixture thereof equivalent to intravenous administration of 0.1 mg to 0.8 mg of a
4 hydrochloride salt of an opioid antagonist, wherein said opioid antagonist is naloxone,
5 naltrexone, methylnaltrexone, nalmefene, nalorphine, levalorphan, oxycodone or buprenorphine,
6 and (b) an amount of nalbuphine free base, hydrochloride salt, prodrug or mixture thereof that
7 results in greater analgesia than administration of either said opioid antagonist free base,
8 prodrug, salt, or mixture thereof or said nalbuphine alone.

1 231. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, and opioid antagonist hydrochloride free base, prodrug, salt, or
3 mixture thereof are administered in amounts equivalent to intravenous administration of 6.25
4 to 30 times greater in weight of nalbuphine hydrochloride salt than the opioid antagonist
5 hydrochloride salt.

1 232. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, and opioid antagonist hydrochloride free base, prodrug, salt, or
3 mixture thereof are administered in amounts equivalent to intravenous administration of 6.25
4 to 25 times greater in weight of nalbuphine hydrochloride salt than opioid antagonist
5 hydrochloride salt.

1 233. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, and opioid antagonist hydrochloride free base, prodrug, salt, or
3 mixture thereof are administered in amounts equivalent to intravenous administration of 6.25
4 to 20 times greater in weight of nalbuphine hydrochloride salt than opioid antagonist
5 hydrochloride salt.

1 234. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, and opioid antagonist hydrochloride free base, prodrug, salt, or
3 mixture thereof are administered in amounts equivalent to intravenous administration of 10 to
4 20 times greater in weight of nalbuphine hydrochloride salt than opioid antagonist
5 hydrochloride salt.

1 235. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, and opioid antagonist hydrochloride free base, prodrug, salt, or
3 mixture thereof are administered in amounts equivalent to intravenous administration of 5 to
4 10 times greater in weight of nalbuphine hydrochloride salt than opioid antagonist
5 hydrochloride salt.

1 236. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 1 mg to 30 mg of nalbuphine hydrochloride salt.

1 237. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 1 mg to 20 mg of nalbuphine hydrochloride salt.

1 238. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 1 mg to 10 mg of nalbuphine hydrochloride salt.

1 239. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 1 mg to 6 mg of nalbuphine hydrochloride salt.

1 240. The method of claim 230 wherein the nalbuphine free base, salt,
2 prodrug, or mixture thereof, is administered in an amount equivalent to intravenous
3 administration of 1 mg to 5 mg of nalbuphine hydrochloride salt.

1 241. The method of any of claims 230-240 wherein the opioid antagonist is
2 naloxone.

1 242. The method of claim 241 wherein the amount of naloxone free base,
2 salt, or prodrug is equivalent to intravenous administration of 0.1 mg naloxone hydrochloride
3 salt and the amount of nalbuphine free base, salt, or prodrug is equivalent to intravenous
4 administration of 1.25 mg nalbuphine hydrochloride salt.

1 243. The method of claim 241 wherein the amount of naloxone free base,
2 salt, or prodrug is equivalent to intravenous administration of 0.2 mg naloxone hydrochloride

3 salt and the amount of nalbuphine free base, salt, or prodrug is equivalent to intravenous
4 administration of 2.5 mg nalbuphine hydrochloride salt are administered.

1 244. The method of claim 241 wherein the amount of naloxone free base,
2 salt, or prodrug is equivalent to intravenous administration of 0.4 mg naloxone hydrochloride
3 salt and the amount of nalbuphine free base, salt, or prodrug is equivalent to intravenous
4 administration of 5 mg nalbuphine hydrochloride salt are administered.

1 245. The method of claim 241 wherein the amount of naloxone free base,
2 salt, or prodrug is equivalent to intravenous administration of 0.8 mg naloxone hydrochloride
3 salt and the amount of nalbuphine free base, salt, or prodrug is equivalent to intravenous
4 administration of 10 mg nalbuphine hydrochloride salt are administered.

1 246. The method of claim 230 wherein the method of mucosal
2 administration is intranasally.

1 247. The method of claim 230 wherein the method of mucosal
2 administration is pulmonary.

1 248. A method of treating pain comprising mucosally administering to an
2 individual in need of said treatment (a) a first amount of an opioid antagonist as a free base,
3 prodrug, salt, or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone,
4 methylnaltrexone, nalmeferone, nalorphine, levalorphan, oxycodone or cyprenorphine, and (b) a
5 second amount of nalbuphine as a free base, salt, prodrug or mixture, wherein said first
6 amount and said second amount are equivalent to intravenous administration of a weight ratio
7 of 1 to 12.5 of said opioid antagonist free base and nalbuphine free base and wherein said
8 administration results in greater analgesia than administration of either said opioid antagonist
9 or said nalbuphine alone.

1 249. The method of claim 248 wherein said second amount is equivalent to
2 intravenous administration of 1 mg to 30 mg of nalbuphine hydrochloride salt.

1 250. The method of claim 248 wherein said second amount is equivalent to
2 intravenous administration of 1 mg to 20 mg of nalbuphine hydrochloride salt.

1 251. The method of claim 248 wherein said second amount is equivalent to
2 intravenous administration of 1 mg to 10 mg of nalbuphine hydrochloride salt.

1 252. The method of claim 248 wherein said second amount is equivalent to
2 intravenous administration of 1 mg to 5 mg of nalbuphine hydrochloride salt.

1 253. The method of claim 248 wherein the opioid antagonist is naloxone
2 hydrochloride salt or an equivalent amount of free base, non-hydrochloride salt, prodrug, or
3 mixture thereof.

1 254. The method of claim 253 wherein said first amount is an amount of
2 naloxone free base, salt, or prodrug equivalent to intravenous administration of 0.1 mg
3 naloxone hydrochloride salt and said second amount is equivalent to intravenous
4 administration of 1.25 mg nalbuphine hydrochloride salt.

1 255. The method of claim 253 wherein said first amount is an amount of
2 naloxone free base, salt, or prodrug equivalent to intravenous administration of 0.2 mg
3 naloxone hydrochloride salt and said second amount is equivalent to intravenous
4 administration of 2.5 mg nalbuphine hydrochloride salt.

1 256. The method of claim 253 wherein said first amount is an amount of
2 naloxone free base, salt, or prodrug equivalent to intravenous administration of 0.4 mg
3 naloxone hydrochloride salt and said second amount is equivalent to intravenous
4 administration of 5 mg nalbuphine hydrochloride salt.

1 257. The method of claim 253 wherein said first amount is an amount of
2 naloxone free base, salt, or prodrug equivalent to intravenous administration of 0.8 mg
3 naloxone hydrochloride salt and said second amount is equivalent to intravenous
4 administration of 10 mg nalbuphine hydrochloride salt.

1 258. The method of claim 253 wherein said first amount is an amount of
2 naloxone free base, salt, or prodrug equivalent to intravenous administration of 1.6 mg
3 naloxone hydrochloride salt and said second amount is equivalent to intravenous
4 administration of 20 mg nalbuphine hydrochloride salt.

1 259. The method of claim 253 wherein said first amount is an amount of
2 naloxone free base, salt, or prodrug equivalent to intravenous administration of 2.0 mg
3 naloxone hydrochloride salt and said second amount is equivalent to intravenous
4 administration of 30 mg nalbuphine hydrochloride salt.

1 260. The method of claim 253 wherein the method of mucosal
2 administration is intranasally.

1 261. The method of claim 253 wherein the method of mucosal
2 administration is pulmonary.

1 262. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) a first amount of an opioid antagonist as a free base, prodrug, salt,
3 or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone,
4 nalmeferone, nalorphine, levorphanol, oxycodone or buprenorphine, and (b) a second amount
5 of nalbuphine as a free base, salt, prodrug or mixture, wherein said first amount and said
6 second amount are equivalent to intravenous administration of a weight ratio of said opioid
7 antagonist free base and said nalbuphine free base that is 1:6.25 to 1:49 and wherein said
8 administration results in greater analgesia than administration of either said opioid antagonist
9 or said nalbuphine alone, provided that 5 mg nalbuphine free base or an equivalent amount of
10 nalbuphine hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof, is not
11 intravenously administered with 0.4 mg naloxone free base or equivalent amount of naloxone
12 hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof.

1 263. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) a first amount of an opioid antagonist as a free base, prodrug, salt,
3 or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone,
4 nalmeferone, nalorphine, levorphanol, oxycodone or buprenorphine, and (b) a second amount
5 of nalbuphine as a free base, salt, prodrug or mixture, wherein said first amount and said
6 second amount are equivalent to intravenous administration of a weight ratio of said opioid
7 antagonist free base and said nalbuphine free base that is 1:6.25 to 1:7 and wherein said
8 administration results in greater analgesia than administration of either said opioid antagonist
9 or said nalbuphine alone.

1 264. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) a first amount of an opioid antagonist as a free base, prodrug, salt,
3 or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone,
4 nalmeferone, nalorphine, levorphanol, oxycodone or buprenorphine, and (b) a second amount
5 of nalbuphine as a free base, salt, prodrug or mixture, wherein said first amount and said
6 second amount are equivalent to intravenous administration of a weight ratio of said opioid

antagonist free base and said nalbuphine free base that is 1:7 to 1:9 and wherein said administration results in greater analgesia than administration of either said opioid antagonist or said nalbuphine alone.

265. A method of treating pain comprising administering to an individual in need of said treatment (a) a first amount of an opioid antagonist as a free base, prodrug, salt, or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone, nalmeferone, nalorphine, levallorphan, oxycodone or buprenorphine, and (b) a second amount of nalbuphine as a free base, salt, prodrug or mixture, wherein said first amount and said second amount are equivalent to intravenous administration of a weight ratio of said opioid antagonist free base and said nalbuphine free base that is 1:9 to 1:11 and wherein said administration results in greater analgesia than administration of either said opioid antagonist or said nalbuphine alone.

266. A method of treating pain comprising administering to an individual in need of said treatment (a) a first amount of an opioid antagonist as a free base, prodrug, salt, or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone, nalmeferone, nalorphine, levallorphan, oxycodone or buprenorphine, and (b) a second amount of nalbuphine as a free base, salt, prodrug or mixture, wherein said first amount and said second amount are equivalent to intravenous administration of a weight ratio of said opioid antagonist free base and said nalbuphine free base that is 1:11 to 1:13 and wherein said administration results in greater analgesia than administration of either said opioid antagonist or said nalbuphine alone, provided that 5 mg nalbuphine free base or an equivalent amount of nalbuphine hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof, is not intravenously administered with 0.4 mg naloxone free base or equivalent amount of naloxone hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof.

267. A method of treating pain comprising administering to an individual in need of said treatment (a) a first amount of an opioid antagonist as a free base, prodrug, salt, or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone, nalmeferone, nalorphine, levallorphan, oxycodone or buprenorphine, and (b) a second amount of nalbuphine as a free base, salt, prodrug or mixture, wherein said first amount and said second amount are equivalent to intravenous administration of a weight ratio of said opioid antagonist free base and said nalbuphine free base that is 1:13 to 1:15 and wherein said

8 administration results in greater analgesia than administration of either said opioid antagonist
9 or said nalbuphine alone.

1 268. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) a first amount of an opioid antagonist as a free base, prodrug, salt,
3 or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone,
4 nalmeferone, nalorphine, levalorphan, oxycodone or buprenorphine, and (b) a second amount
5 of nalbuphine as a free base, salt, prodrug or mixture, wherein said first amount and said
6 second amount are equivalent to intravenous administration of a weight ratio of said opioid
7 antagonist free base and said nalbuphine free base that is 1:15 to 1:20 and wherein said
8 administration results in greater analgesia than administration of either said opioid antagonist
9 or said nalbuphine alone.

1 269. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) a first amount of an opioid antagonist as a free base, prodrug, salt,
3 or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone,
4 nalmeferone, nalorphine, levalorphan, oxycodone or buprenorphine, and (b) a second amount
5 of nalbuphine as a free base, salt, prodrug or mixture, wherein said first amount and said
6 second amount are equivalent to intravenous administration of a weight ratio of said opioid
7 antagonist free base and said nalbuphine free base that is 1:20 to 1:30 and wherein said
8 administration results in greater analgesia than administration of either said opioid antagonist
9 or said nalbuphine alone.

1 270. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) a first amount of an opioid antagonist as a free base, prodrug, salt,
3 or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone, methylnaltrexone,
4 nalmeferone, nalorphine, levalorphan, oxycodone or buprenorphine, and (b) a second amount
5 of nalbuphine as a free base, salt, prodrug or mixture, wherein said first amount and said
6 second amount are equivalent to intravenous administration of a weight ratio of said opioid
7 antagonist free base and said nalbuphine free base that is 1:30 to 1:49 and wherein said
8 administration results in greater analgesia than administration of either said opioid antagonist
9 or said nalbuphine alone.

1 271. The method of claim 262, wherein the second amount of nalbuphine
2 hydrochloride salt is 1 mg to 5 mg, or an equivalent amount of nalbuphine free base, prodrug,
3 non-hydrochloride salt, or a mixture of one or more thereof.

1 272. The method of claim 262, wherein the second amount of nalbuphine
2 hydrochloride salt is 1 mg to 10 mg, or an equivalent amount of nalbuphine free base,
3 prodrug, non-hydrochloride salt, or a mixture of one or more thereof.

1 273. The method of claim 262, wherein the second amount of nalbuphine
2 hydrochloride salt is 1 mg to 20 mg, or an equivalent amount of nalbuphine free base,
3 prodrug, non-hydrochloride salt, or a mixture of one or more thereof.

1 274. The method of claim 262, wherein the second amount of nalbuphine
2 hydrochloride salt is 1 mg to 30 mg, or an equivalent amount of nalbuphine free base,
3 prodrug, non-hydrochloride salt, or a mixture of one or more thereof.

1 275. The method of claim 262, wherein the method of administration is
2 intranasal.

1 276. The method of claim 262, wherein the method of administration is
2 intravenous.

1 277. The method of claim 262, wherein the method of administration is
2 pulmonary.

1 278. The method of claim 262, wherein the method of administration is
2 transdermal.

1 279. The method of claim 262, wherein the method of administration is
2 mucosal.

1 280. A method of treating pain comprising mucosally administering to an
2 individual in need of said treatment (a) 0.02 mg to 8 mg of a hydrochloride salt of an opioid
3 antagonist or an equivalent amount of opioid antagonist free base, prodrug, non-
4 hydrochloride salt, or mixture thereof, wherein said opioid antagonist is naloxone, naltrexone,
5 methylnaltrexone, nalmefene, nalorphine, levalorphan, oxylorphan or cyprenorphine, and (b)
6 an amount of nalbuphine free base, hydrochloride salt, prodrug, non-hydrochloride salt or

7 mixture thereof that results in greater analgesia than administration of either said opioid
8 antagonist hydrochloride salt or said nalbuphine alone.

1 281. A pharmaceutical composition comprising (a) 0.02 mg to 8 mg of a
2 hydrochloride salt of an opioid antagonist or an equivalent amount of opioid antagonist free
3 base, prodrug, non-hydrochloride salt, or mixture thereof, wherein said opioid antagonist is
4 naloxone, naltrexone, methylnaltrexone, nalmefene, nalorphine, levalorphan, oxylorphan or
5 cyprenorphine; (b) an amount of nalbuphine free base, nalbuphine salt, nalbuphine prodrug,
6 or mixture thereof that results in greater analgesia than administration of the nalbuphine
7 ingredient or the opioid antagonist ingredient alone; and (c) a pharmaceutically acceptable
8 carrier, said pharmaceutical composition being formulated for mucosal administration.

1 282. A method of treating pain comprising mucosally administering to an
2 individual in need of said treatment (a) an amount of an opioid antagonist free base, prodrug,
3 salt, or mixture thereof equivalent to intravenous administration of 0.02 mg to 8 mg of a
4 hydrochloride salt of an opioid antagonist, wherein said opioid antagonist is naloxone,
5 naltrexone, methylnaltrexone, nalmefene, nalorphine, levalorphan, oxylorphan or cyprenorphine,
6 and (b) an amount of nalbuphine free base, hydrochloride salt, prodrug or mixture thereof that
7 results in greater analgesia than administration of either said opioid antagonist free base,
8 prodrug, salt, or mixture thereof or said nalbuphine alone.

1 283. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) from 0.02 to 8 mg of a hydrochloride salt of naloxone or an
3 equivalent amount of naloxone free base, prodrug, non-hydrochloride salt, or mixture thereof;
4 and (b) from 1 to 2.5 mg of nalbuphine hydrochloride, or an equivalent amount of nalbuphine
5 free base, prodrug, non-hydrochloride salt or mixture thereof.

1 284. A method of treating pain comprising administering to an individual in
2 need of said treatment (a) from 0.02 to 8 mg of a hydrochloride salt of naloxone or an
3 equivalent amount of naloxone free base, prodrug, non-hydrochloride salt, or mixture thereof;
4 and (b) from 8.5 to 30 mg of nalbuphine hydrochloride, or an equivalent amount of
5 nalbuphine free base, prodrug, non-hydrochloride salt or mixture thereof.

1 285. A pharmaceutical composition for treating pain comprising (a) 0.02 mg
2 to 8 mg of a hydrochloride salt of an opioid antagonist or an equivalent amount of opioid
3 antagonist free base, prodrug, non-hydrochloride salt, or mixture thereof, wherein said opioid

4 antagonist is naloxone, naltrexone, methylnaltrexone, nalmefene, nalorphine, levalorphan,
5 oxylorphan or cyprenorphine, (b) an amount of nalbuphine free base, hydrochloride salt,
6 prodrug, non-hydrochloride salt or mixture thereof that results in greater analgesia than
7 administration of either said opioid antagonist hydrochloride salt or said nalbuphine alone;
8 and (c) a pharmaceutically acceptable carrier; provided that said composition formulated for
9 intravenous administration does not comprise 5 mg nalbuphine free base with 0.4 mg
10 naloxone free base.

1 286. A composition for treating pain comprising (a) 0.02 mg to 8 mg of a
2 hydrochloride salt of an opioid antagonist or an equivalent amount of opioid antagonist free
3 base, prodrug, non-hydrochloride salt, or mixture thereof, wherein said opioid antagonist is
4 naloxone, naltrexone, methylnaltrexone, nalmefene, nalorphine, levalorphan, oxylorphan or
5 cyprenorphine; (b) an amount of a free base, hydrochloride salt, prodrug, non-hydrochloride
6 salt or mixture thereof of a kappa- opioid, that results in greater analgesia than administration
7 of either said opioid antagonist hydrochloride salt or said kappa-opioid, wherein the kappa-
8 opioid is pentazocine, butorphanol, ketazocine, ethylketazocine, dezocine, bremazocine, a
9 benzacetamide derivative, a phenothiazine derivative, a thiazine derivative, or a
10 benzodiazepine derivative; and (c) a pharmaceutically acceptable carrier; provided that said
11 composition formulated for intravenous administration does not comprise 60 mg of
12 pentazocine free base or an equivalent amount of pentazocine hydrochloride salt, non-
13 hydrochloride salt, prodrug, or mixture thereof and 0.4 mg naloxone free base or equivalent
14 amount of naloxone hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof
15 and provided that said composition formulated for oral administration does not comprise 50
16 mg of pentazocine free base or an equivalent amount of pentazocine hydrochloride salt, non-
17 hydrochloride salt, prodrug, or mixture thereof and 0.5 mg naloxone free base or equivalent
18 amount of naloxone hydrochloride salt, non-hydrochloride salt, prodrug, or mixture thereof.